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Correlation between coprecipitation reaction course and magneto-structural properties of iron oxide nanoparticles

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HIGHLIGHTS

- Uniform and highly crystalline iron oxide nanoparticles are prepared by coprecipitation method.
- We report mechanisms of nanoparticles nucleation and growth depending on synthetic parameters.
- Instant homogeneous nucleation and slow crystal growth account for nanoparticles uniformity.
- Rapid heating of nanoparticles dispersion in alternating magnetic field at moderate amplitude is obtained.
- High heating ability is determined by to the enhancement of energy barrier of magnetization reversal.

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ABSTRACT

The effect of coprecipitation reaction course on the magneto-structural properties of iron oxide nanoparticles and, as a consequence, on their heating ability in alternating magnetic fields allowed in magnetic hyperthermia was studied. The parameters of coprecipitation reaction are chosen to ensure the repeatability of nanoparticles features: narrow size distribution, high crystallinity, and magnetic properties. It is established that the reaction should be carried out in an alkaline medium with slow addition of a solution of iron (II) and iron (III) salts to excess alkali. This provides a simultaneous homogeneous nucleation and a rapid growth of nanocrystals during the first minutes of the reaction. After that the reaction proceeds to the stage of slow growth of nanoparticles, which continues up to the complete exhaustion of the solution of salts. Nanoparticles unite in aggregates during the synthesis. The particles in aggregates are characterized by average size of 13 nm and polydispersity index 0.3, mixed phase composition including pure phase magnetite and the products of its oxidation (non-stoichiometric magnetite and maghemite nanoparticles). Material displays magnetization saturation of 56 emu g^{-1}, non-zero hysteresis and distinct sextets on Mössbauer spectrum at room temperature. A glycerol dispersion of aggregated magnetic nanoparticles provides a temperature increase from 37 °C to 45 °C within tens of seconds under exposure to alternating magnetic field allowed for application in magnetic hyperthermia. The high heating ability is associated with interparticle magnetic interactions within aggregates leading to the enhancement of energy barrier of magnetization reversal.

1. Introduction

Today, a lot of research is carried out on the development of a magnetic material (mediator) for Magnetic Hyperthermia (MH) [1–3]. In this non-surgical cancer treatment method the magnetic material incorporated inside the tumor accumulates the energy of alternating magnetic field (AMF) and transfers it into heat. In this way it is possible to achieve hyperthermia temperatures from 42 °C to 45 °C, which are cytotoxic for cancer cells, to localize the heating in the tumor and to reduce the treatment time. The efficiency of hyperthermia is characterized by either specific absorption rate (SAR), which is defined as the power absorbed per mass of tissue, or

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by the specific loss power (SLP) of the mediator at a certain frequency and strength of the magnetic field, which is the power eliminated by a gram of magnetic mediator. For MH to be used in clinical practice, the first challenge is to develop a mediator with maximum SAR/SLP at frequencies (f) and amplitudes (H) of an AMF that are allowed for medical application. The safe upper limit for the field frequency and amplitude is accepted to be $(H \cdot f)_{crit} \leq 4.85 \cdot 10^8$ A m^{-1} s^{-1}, i.e. $H \leq 15$ kA m^{-1} and $0.05 \leq f \leq 1.5$ MHz [4]. Although magnetic materials with high magneto-crystalline anisotropy, such as cobalt and cobalt-containing ferrites, have higher response to AMF, the main preference is given to nanoparticles of magnetic iron oxides (magnetite and maghemite) due to their biocompatibility and high magnetic moment [5–8].

The phenomena underlying the heat generation in iron oxide magnetic nanoparticles exposed to AMF are discussed in a comprehensive papers/reviews of Dennis and Ivkov [9], Dutz and Hergt [10], Raikher and Stepanov [11], Carrey, Mehdaoui and Respaud [12]. It is established that maximum heat in AMF provides uniform single-domain nanoparticles with optimal anisotropy in which the relaxational losses account for heat generation. Two types of magnetization relaxation are possible: Nèel and Brown relaxation. However, when the particles are immobilized in a viscous medium, for example, when they are distributed in a tumor tissue, the Brown relaxation is suppressed [11,13]. If the energy barrier of magnetization reversal ($\Delta E = K \cdot V$, where K is anisotropy energy and V is volume of nanoparticle) is high enough, the magnetic moment lags to orient over the field direction and the energy loss occurs. It is assumed that a key parameter determining the heating efficiency of nanoparticles is anisotropy, which is defined by the competition between several anisotropies: (1) magneto-crystalline anisotropy, which is governed by the symmetry of the crystal lattice; (2) shape anisotropy, which is controlled by magnetostatic energy arising from demagnetizing fields; (3) anisotropy of imposed stress (induced magnetic anisotropy); (4) surface anisotropy related to the breaking of the symmetry and reduction in the nearest neighbor coordination at the surface, (5) anisotropy of collective state associated with interparticle magnetic interactions [14].

The highest reported up-today values of SLP of several kW g^{-1} are obtained for water dispersions of nanoparticles subjected to AMFs with amplitude far above the allowed limit [15–19]. It is known that in low viscosity media two relaxation mechanisms account for heat generation. Therefore, there is still a need for development of nanoparticles with high losses in allowed AMFs and in viscous media.

Chemical methods for obtaining iron oxide nanoparticles in the SD size range can be generally divided into two groups according to the reaction medium: organic or aqueous. Organic methods are based on thermal decomposition of organo-metallic precursors in a high-boiling-point solvent and provide aggregation-free, monocrystalline and monodisperse nanoparticles in the size range 4–50 nm [20–23]. However, there is a high probability for the formation of nanoparticles with high degree of disorder due to the two-step seeded growth synthetic procedure used in this method, which leads to a low heating potential of nanoparticles in an AMF [24]. Furthermore, nanoparticles obtained by organic methods have a surfactant coating, which affects their biocompatibility. Alternatively, aqueous method of synthesis (i.e., coprecipitation of iron (II) and iron (III) salts and precipitation of iron (II) salt with further oxidation) offers an opportunity to obtain biocompatible iron oxide nanoparticles from aqueous solutions of non-toxic initial reagents at temperatures not exceeding 100 °C [25–27]. The main disadvantages of this method reported in the literature are the broad particle size distribution and poor repeatability of nanoparticles properties [25,27].

The main factors influencing the magneto-structural properties of iron oxide nanoparticles obtained by coprecipitation have been intensively discussed in the literature; these are the iron (II) to iron (III) molar ratio, the type of the precipitant, the pH of the reaction medium, the reaction temperature, the presence of surfactants, the reagents addition rate, agitation, etc. [25,28–30]. However, only little attention is given to the study of the mechanisms of nucleation and growth of magnetite from a solution, although these mechanisms are of considerable importance for the optimization of morphological, crystallographic, and magnetic characteristics of nanoparticles.

The production of iron oxide by coprecipitation method is usually described by the following reactions:

$$Fe^{+2} + 2Fe^{+3} + 8OH^- \rightarrow Fe(OH)_2 + 2Fe(OH)_3, \tag{1}$$

$$Fe(OH)_2 + 2Fe(OH)_3 + 8OH^- + 8H^+ \rightarrow Fe_3O_4 + 12H_2O. \tag{2}$$

However, this is a simplified representation of the magnetite production process. In [28,31,32], the authors have shown that magnetite is formed as a product in the conversion of iron oxyhydroxides, rather than by a direct reaction between Fe^{2+} and Fe^{3+} cations in an aqueous medium. In this work we demonstrate the impact of coprecipitation reaction course on the mechanism of magnetic iron oxide nanoparticle formation, which determines the magneto-structural properties and the heating ability of nanoparticles in AMFs. The synthesis protocol was established that allowed to obtain uniform magnetic iron oxide nanoparticles that provide high heating efficiency in the viscous dispersion media in AMFs approved for application in MH.

2. Experimental

2.1. Reactants

All reactants used in this work (ferrous and ferric chlorides, ammonium hydroxide, glycerol) were analytical grade and were used as purchased from Sigma–Aldrich. Distilled water used for preparing the solutions was deoxygenated by argon bubbling for an hour.

2.2. Preparation of iron oxide magnetic nanoparticles

Magnetic particles were prepared by coprecipitation of ferrous and ferric salts in an alkaline medium. 300 ml of 0.38 M ammonium hydroxide solution, used as a precipitation agent, was mixed with a 30 ml of ferrous chloride tetrahydrate and ferric chloride hexahydrate solution with a molar ratio of Fe (II)/Fe (III) = 0.0125 mol/0.025 mol = 0.5, which was used as a source of iron. This molar ratio of iron (II) to iron (III) is equal to that of stoichiometric magnetite. The reaction was performed in an argon atmosphere to prevent the oxidation of Fe^{2+} ions and to keep the Fe (II)/Fe (III) molar ratio constant. The reaction was performed in a round-bottom flask. The temperature of the reaction mixture was maintained at 70 °C with a continuous stirring speed of 700 rpm. The synthesis was carried out in two different ways.

In the first case, ammonium hydroxide solution was added dropwise (2 ml min^{-1}) to ferrous and ferric chloride solution (Sample I). In the second case, the precipitation was performed with the same solutions and under the same conditions, but the salts solution was added to the base solution (0.2 ml min^{-1}) (Sample II). In both cases, after the addition of the reagents was completed, the system was left for an hour at 70 °C and stirring at 700 rpm. The black powders of iron oxide nanoparticles formed in